

LUD 5353.5 DIV JEL/NDH (10016355)

The examiner points to differences in nucleic acid residues between SEQ ID NOS: 13 & 14 in support of this.

The holding is traversed.

The examiner's attention is drawn to the fact that SEQ ID NOS: 13 & 14 are presented such that coding regions are shown in triplet form, and non-coding regions in groups in ten nucleotides. The coding region, or ORFs, for SEQ ID NOS: 13 & 14 run from nucleotides 625-1578, respectively.

The alignment presented by the examiner shows a total of 2 nucleotide differences within the ORF, at 708 ("GCA" vs "GCS"), and at 1141 ("ACC" vs "GCC"). The change from GCA to GCG is a silent mutation. Both codons stand for Alanine. A change in GCC v ACC is not silent; however, the end result is one amino acid difference within the protein, i.e., Ala (GCC) v Thr (ACC). The change does not impact the TRA known for MAGE-4. See, e.g., U.S. Patent No. 5,405,940, a copy of which is attached. Further, these de minimus differences, taken with the three additional changes shown over 2500 nucleotides (a total of 5 out of 2530, or less than .004%), does not impact the claimed invention. Molecules which hybridize to SEQ ID NO: 13 should hybridize to SEQ ID NO: 14 under the recited conditions, and vice versa. There is absolutely no reason to conclude the contrary.

As such, applicants do not see the restriction as proper, traverse it, and content that the claims should be considered as one.

Allowance of this application is believed proper and is requested.

Respectfully submitted,

FULBRIGHT & JAWORSKI, L.L.P.



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Registration No. 30,946

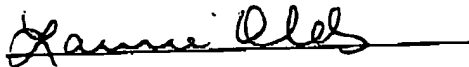
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LUD-5353.5 JEL/NDH (10016358)

VIA FACSIMILE

I hereby certify that this correspondence is being facsimile transmitted to the Commissioner of Patents and Trademarks, Washington, D.C. 20231 on November 25, 2002.

Fulbright & Jaworski L.L.P.



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Applicant : Beatrice GAUGLER et al.
Serial No. : 09/579,543
Filed : May 26, 2000
For : ISOLATED NUCLEIC ACID MOLECULES CODING FOR
TUMOR REJECTION ANTIGEN PRECURSOR MAGE-4
AND 41 AND USES THEREOF
Art Unit : 1642
Examiner : Alana Harris

November 25, 2002

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

SHOWING OF CHANGES

Page 35, line 13-page 36, line 3:

Melanoma cell line LB-33-MEL was tested. Total mRNA from the cell line was used to prepare cDNA, which was then amplified with oligos CHO9, which is the complement of nucleotides 4526 of 4545 of SEQ ID NO: 8: (ACTCAGCTCCTCCCAGATTT) and CHO10, which is nucleotides 4180-4195 of SEQ ID NO: 8: (GAAGAGGAGGGGCCAAG). These oligos correspond to regions of exon 3 that are common to previously described mage 1, 2 and 3.

To do this, 1 µg of RNA was diluted to a total volume of 20 µl, using 2 µl of 10x buffer, 2 µl of each of 10 mM dNTP, 1.2 µl of 25 mM MgCl₂, 1 µl of an 80 mM solution of CHO9, described of an 80 mM solution of CHO9, described supra, 20 units of RNAsin, and 200 units of M-MLV reverse transcriptase. This was followed by incubation for 40 minutes at 42°C. PCR amplification followed, using 8 µl of 10x PCR buffer, 4.8 µl of 25 mM MgCl₂, 1 µl of CHO10, 2.5 units of *Thermus aquaticus* ("Taq") polymerase, and water to a total volume of 100 µl.

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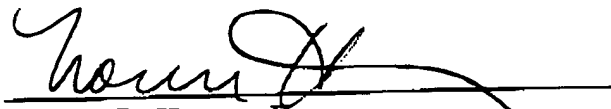
Amplification was then carried out for 30 cycles (1 minute at 94°C; 2 minutes at 52°C, 3 minutes at 72°C). Ten µl of each reaction were then size fractionated on agarose gel, followed by nitrocellulose blotting. The product was found to hybridize with oligonucleotide probe CHO18, which is nucleotides 4201-4218 of SEQ ID NO: 8: (TCTTGTATCCTGGAGTCC). This probe identified mage 1 but not mage 2 or 3. However, the product did not hybridize to probe SEQ 4, which is the complement of nucleotides 4349-4366 of SEQ ID NO: 8: (TTGCCAAGATCTCAGGAA). This probe also binds mage 1 but 2 and 3. This indicated that the PCR product contained a sequence that differed from mage 1, 2 and 3. Sequencing of this fragment also indicated differences with respect to mage 4 and 5. These results indicate a sequence differing from previously identified mage 1, 2, 3, 4 and 5, and is named mage 6.

Page 36, lines 20-26:

To do this, and using standard protocols, cells normally insensitive to anti-E/CTLs were incubated with the synthetic peptides derived from Exon 3.1. Using the CTL lytic assays described supra on P815A, and a peptide concentration of 3 mM, the peptide Glu-Ala-Asp-Pro-Thr-Gly-His-Ser-Tyr (SEQ ID NO: 26) was shown to be best. The assay showed lysis of 30%, indicating conferring of sensitivity to the anti-E CTL.

Respectfully submitted,

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